DETAILED ACTION

Status of the Claims

Applicant's response dated 6/16/2011 to the non-final rejection mailed 12/16/2010 has been entered. Claims 1, 15, 16, 26, and 28 have been amended. New claims 29 and 30 have been added. Support is found in the specification as filed for these amendments. Claims 22-24 and 27 are canceled.

Claims 1-21, 25, 26, and 28-30 are under current examination.

Withdrawn Claim Rejections

The rejection of claims 1, 3, 15, and 16 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 and 20 of copending Application No. 11908708 is withdrawn in light of Applicant's amendments to the claims.

The rejection of claims 1-8, 10, 11, 14-19, 21, and 25-28 under 35 U.S.C. 103(a) as being unpatentable over Forster as evidenced by Lau and in view of Ludwig is withdrawn in view of Applicant's amendments to the claims.

The rejection of claim 20 under 35 U.S.C. 103(a) as being unpatentable over Forster as evidenced by Lau and in view of Ludwig and further in view of Whitehead is withdrawn in view of Applicant's amendments to the claims.

The rejection of claim 12 under 35 U.S.C. 103(a) as being unpatentable over Forster as evidenced by Lau and in view of Ludwig and further in view of IVS Annual Index of Veterinary Products is withdrawn in view of Applicant's amendments to the claims.

The rejection of claim 13 under 35 U.S.C. 103(a) as being unpatentable over Forster as evidenced by Lau and in view of Ludwig and further in view of Sanyal et al. is withdrawn in view of Applicant's amendments to the claims.

The rejection of claim 9 under 35 U.S.C. 103(a) as being unpatentable over Forster as evidenced by Lau and in view of Ludwig and further in view of Jeannin is withdrawn in view of Applicant's amendments to the claims.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-20 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites in line 5 that the reduction is in the level of "resistant parasites" in a ruminant animal. Although the specification addresses some non-limiting characteristics of parasites which may be considered "resistant" (see page 2, line 20), the specification does not clearly define or otherwise limit which parasites may be included (or, excluded, for that matter) by the terminology in the claims. Consequently, the term "resistant" appears subjective, and it is unclear to the skilled artisan as to what would infringe the rejected claims. Moreover the claim does not make clear to what the ruminant animals are resistant. Appropriate clarification is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8, 10, 11, 14-19, 21, 25, 26, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Forster et al. (AU 52162/96 A, filed May 1996, see IDS filed 4/21/2006) as evidenced by Lau et al. (WO

2004/069242 A) and in view of Ludwig et al. (US 4,331,652, issued May 1982) and Chou (US 4,066,754, issued Jan. 3, 1978).

The pending claims embrace a particular method of reducing parasites in ruminant animals.

Regarding claims 1, 2, 6-8, 10, and 26-28, Forster et al. teaches synergistic compositions of benzimidazoles (microtubule disruptors) and abamectin (a macrocyclic lactone that is a chloride channel blocker) as anthelmintics including nematocidal compositions. Benzimidazoles are generally microtubule disruptors, whereas abamectin is a chloride channel blocker. Thus Forster clearly taught compositions comprising anthelmintics with different chemical groups and activities as required by claims 1 and 2, respectively. The formulation effectively targets ascarids, hookworms, whipworms, and heartworms upon the combination of abamectin (dosage between 5 and 15 ug per kg of animal body weight) and benzimidazole or pro-benzimidazole (dosage between 15 and 30 mg per kg of animal body weight) (see page 3, paragraph 3). As to claim 21, the first Example of the invention demonstrates a palatable tablet in chewable form as a delivery device (see page 4, paragraph 4).

Similarly, Lau et al. also teach anthelmintically effective compositions for treating parasitic infections in animals (see abstract, in particular). As to claim 1, Lau et al. establishes that the anthelmintic active agents of Forster necessarily would have been active against parasites in ruminant animals such as sheep (see page 3, last paragraph). Further regarding claims 4-6, Lau et al. teach anthelmintic compositions comprising benzimidazoles, macrocyclic lactones, and

a therapeutically acceptable carrier wherein the formulation demonstrates "excellent control (>99.9% reduction) of a mixed gastrointestinal strongyle burden as assessed" (page 17, paragraph 1). Therefore, the implementation of these actives necessarily would have had the instantly claimed efficacy.

Regarding claim 1, Forster et al. do not disclose an intra-ruminal bolus delivery device or a stepwise method as instantly claimed.

Nonetheless, Ludwig et al. teach the controlled release of an anthelmintic agent from a bolus (see column 8, lines 48 - column 9, line 7) into the rumen of a ruminant animal (see column 7, line 56). Ludwig teaches that the parasiticide provides uniform protection against the parasites for a predetermined period of time (see column 2, lines 17-24). The payout periods were specifically monitored up to 14 days (see Table 1, column 8, lines 55-65). The bolus is to be administered orally (see column 7, line 55).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the bolus device and method of administering anthelmintic agents to administer the synergistic anthelmintic compositions of Forster et al. One would have been motivated to do so since Ludwig teaches that the advantages of the bolus device include the lack of undesired chemical residues in animals used for human food production as well as the advantage that the controlled release formulation does not expose the host animal to lethal doses of the active agent (see column 2, lines 8-20).

Further regarding claims 1, 15, and 16, the aforementioned references do not teach that the duration of exposure comprises at least 3 days but no more

than 6 to 8 days as required by the claim amendments. However, Chou is directed to a slow release bolus for the controlled delivery of veterinary medicaments such as antihelmintics in ruminant animals including sheep (see abstract, in particular; see also, column 1, line 17; column 2, lines 65-68, and claim 14). Chou specifies that the boluses release a therapeutically active substance for a period of up to about 15 days in duration (see column 1, lines 58-62), including a period preferably of about 4 days (see column 3, line 15; column 6, lines 15 and line 33).

Both Forster and Chou are directed to the controlled delivery of anthelmintic active agents. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to adjust the bolus release duration as taught by Chou (i.e., by adjusting the disintegrant as taught by Chou). One would have been motivated to do so since Chou teaches that this time period for administering an extended release bolus was known to be effective to provide delivery for a case of a disease where only a relatively short period of non-immediate release into the rumen of a ruminant animal would have been desirable. In this case, the bolus would have terminated release by the end of said defined period as recited in claim 26 so as to minimize undesirable drug exposure once the short treatment time of administration (i.e., four days) was met (see Chou column 6, line 32). As to claim 28, it would have been obvious to one of ordinary skill in the art at the time the invention was made to increase the days of administration from four as used in the cited recommendation of Chou to a

number of days not exceeding 15, including 6, 7, or 8 days, as otherwise taught by Chou and to reasonably expect success from doing so.

As to claims 3, 19, and 25, the active agent is administered by uniform controlled release (substantially continuous) (see Ludwig column 6, lines 32-36); it is noted that the instant specification does not provide a definition for a "substantially continuous rate". As to claim 11, Ludwig teaches albendazole as a particular benzimidazole used in Example 10 (see column 13, line 65). As to claim 14, Ludwig teaches sheep as a ruminant animal for which the disclosed dosage is suitable (see column 7, line 53). As to claims 17 and 18, Ludwig teaches the state of the art indicating that the imidazothiazoles known in the art effectively inhibit helminthiasis (helminthes) (see column 3, line 35) and that the invention applies to ectoparasites such as lice, ticks, and fleas (see column 1, line 15).

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Forster et al. (AU 52162/96 A, filed May 1996, see IDS filed 4/21/2006) as evidenced by Lau et al. (WO 2004/069242 A1) and in view of Ludwig et al. (US 4,331,652, issued May 1982) and Chou (US 4,066,754, issued Jan. 3, 1978) as applied above and further in view of Jeannin et al. (US 6,162,820, issued Dec. 19, 2000).

The Forster, Lau, Ludwig, and Chou references are delineated above. Neither Forster nor Ludwig teach the abamectin dosage as in pending claim 9.

Jeannin et al. teaches methods for removing parasites and ectoparasites from mammals (see abstract, in particular). The Jeannin reference indicates that abamectin is among equivalent preferred parasiticides (see column 3, lines 38-40) and that the effective dose administered in the method of the invention is preferably between 0.001, preferentially 0.01, and 100 mg/kg of animal weight or 0.01 to 15 mg/kg/day of endectocide (see column 3, line 65 - column 4, line 3; see also column 6, lines 20-22). It is noted that these ranges include and render obvious the data point (or range) which is "about 0.18 mg/kg/day" of abamectin as recited in claim 30. The Jeannin reference further specifies that the dosage amounts vary in order to maintain a serum level which can be adjusted to combat fleas (lower serum level) or ticks (higher serum level) for an animal of a specified mass (see column 4, lines 2-18).

Both the Forster and Jeannin references are directed to methods of reducing parasite presence. Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to optimize the quantity of abamectin to be administered to the animals per kg of body weight per day, based on the teaching of Jeannin et al., with the reasonable expectation of success. One would have been motivated to do so as it is routine inquiry in the art to minimize cost and harmful side effects while maximizing benefits. See MPEP 2144.05. One would have been motivated to utilize dosage quantities near the lower end of the dosage range specified by Jeannin et al. in order to combat fleas (parasites) by maintaining a relatively low serum level in accordance with Jeannin's teaching.

Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Forster et al. (AU 52162/96 A, filed May 1996, see IDS filed 4/21/2006) as evidenced by Lau et al. (WO 2004/069242 A1) and in view of Ludwig et al. (US 4,331,652, issued May 1982) and Chou (US 4,066,754, issued Jan. 3, 1978) as applied above and further in view of IVS Annual Index of Veterinary Products (see IDS, 5/31/2007).

The teachings of Forster et al., Lau et al., Ludwig et al., and Chou are delineated above. None of these references teaches the particular dosage of albendazole as in pending claim 12.

However, the IVS Annual Index teaches that 4.75 mg/kg of albendazole is an effective dosage quantity for rendering anti-parasitic effects in sheep.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the dosage quantity of albendazole as taught by the IVS Annual Index in the formulations of Forster et al. and Ludwig et al. One would have been motivated to do so in order to impart the known benefits of such a dosage while expecting to minimize harmful side effects of an overdose, particularly since the skilled artisan would have considered the IVS Annual Index a reference source for dosage details associated with known active agents such as anti-parasites, and, more specifically, albendazole.

Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Forster et al. (AU 52162/96 A, filed May 1996, see IDS filed 4/21/2006)

as evidenced by Lau et al. (WO 2004/069242 A1) and in view of Ludwig et al. (US 4,331,652, issued May 1982) and Chou (US 4,066,754, issued Jan. 3, 1978) as applied above, and further in view of Sanyal et al. (Vet. Res. Comm. *20*, 1996, 461-468).

The teachings of Forester et al., Lau et al., Ludwig et al., and Chou are delineated above. None of these references teaches the particular anthelmintic compound that is tricalbendazole.

However, Sanyal et al. teach that tricalbendazole is an effective low-level intraruminal anti-fluke anti-parasite agent (see abstract, in particular).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to substitute tricalbendazole as the anthelmintic agent as taught by Sanyal et al. into the formulations of Forester and Ludwig which also utilize known anthelmintic active agents. One would have been motivated to do so in order to impart the known anti-parasite effects of tricalbendazole as well as its ability to bind to albumin better than nematocidial benzimidazoles such as oxfendazole or fenbendazole (see page 465, Discussion, paragraph 1).

Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Forster et al. (AU 52162/96 A, filed May 1996, see IDS filed 4/21/2006) as evidenced by Lau et al. (WO 2004/069242 A1) and in view of Ludwig et al. (US 4,331,652, issued May 1982) and Chou (US 4,066,754, issued Jan. 3,

1978) as applied above and further in view of Whitehead (US 6,030,637, patented Feb. 2000).

The teachings of Forster et al., Lau et al., Ludwig et al., and Chou are set forth above. These references do not explicitly teach a maximum integral dose as in claim 20.

Nonetheless, Whitehead teaches a bolus of elements, each having a degradable outer sheath and a core of an active formulation (see column 2, line 18) for deposition of active agents to a ruminant (see column 1, line 19; column 1, line 26). More specifically, Whitehead teaches the option of utilizing boli which release the active agent continuously as a function of time (see column 1, line 19). As to claim 20, Whitehead teaches an embodiment of the invention in which a bolus comprising a plurality of discrete bolus elements releases the biologically active material at different respective intervals based on the adapted sheath formulation (see column 4, lines 22-30); further, the drug can be administered in integral units over a few hours to a period of a few months (see column 5, lines 1-10). Therefore, a formulation released in a pulse fashion necessarily has a maximum integral dose.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to incorporate the bolus-related teachings of Whitehead in order to formulate a controlled delivery device for the anthelmintic compositions of Forster et al., Lau et al., and Ludwig et al. One would have been motivated to do so in order to improve the efficacy of the formulation by

controlling the delivery so as to increase dosage or decrease dosage as a function of delivery time as taught by Whitehead.

Claims 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Forster et al. (AU 52162/96 A, filed May 1996, see IDS filed 4/21/2006) as evidenced by Lau et al. (WO 2004/069242 A1) and in view of Ludwig et al. (US 4,331,652, issued May 1982, newly cited) and Chou (US 4,066,754, issued Jan. 3, 1978) as applied above and further in view of IVS Annual Index of Veterinary Products (see IDS, 5/31/2007) and Jeannin et al. (US 6,162,820, issued Dec. 19, 2000).

Forster et al. teaches synergistic compositions of benzimidazoles (microtubule disruptors) and abamectin (a macrocyclic lactone that is a chloride channel blocker) as anthelmintics including nematocidal compositions. Benzimidazoles are generally microtubule disruptors, whereas abamectin is a chloride channel blocker. The formulation effectively targets ascarids, hookworms, whipworms, and heartworms upon the combination of abamectin and benzimidazole or pro-benzimidazole (see page 3, paragraph 3).

Similarly, Lau et al. also teach anthelmintically effective compositions for treating parasitic infections in animals (see abstract, in particular). Lau et al. establishes that the anthelmintic active agents of Forster necessarily would have been active against parasites in ruminant animals such as sheep (see page 3, last paragraph). Lau et al. teach anthelmintic compositions comprising benzimidazoles, macrocyclic lactones, and a therapeutically acceptable carrier

wherein the formulation demonstrates "excellent control (>99.9% reduction) or a mixed gastrointestinal strongyle burden as assessed" (page 17, paragraph 1). Therefore, the implementation of these actives necessarily would have had the instantly claimed efficacy of reducing parasites.

Forster et al. do not disclose an intra-ruminal bolus delivery device or a stepwise method of delivery as instantly claimed.

Nonetheless, Ludwig et al. teach the controlled release of an anthelmintic agent from a bolus (see column 8, lines 48 - column 9, line 7) into the rumen of a ruminal animal (see column 7, line 56). Ludwig teaches that the parasiticide provides uniform protection against the parasites for a predetermined period of time (see column 2, lines 17-24). The payout periods were specifically monitored up to 14 days (see Table 1, column 8, lines 55-65). The bolus is to be administered orally (see column 7, line 55). In addition, the active agent is administered by uniform controlled release (constant) (see Ludwig column 6, lines 32-36) Ludwig teaches albendazole as a particular benzimidazole used in Example 10 (see column 13, line 65) and sheep as ruminant animals for which the disclosed dosage is suitable (see column 7, line 53). Ludwig teaches the state of the art indicating that the imidazothiazoles known in the art effectively inhibit helminthiasis (helminthes) (see column 3, line 35) and that the invention applies to ectoparasites such as lice, ticks, and fleas (see column 1, line 15).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the bolus device and method of administering anthelmintic agents as taught by Ludwig et al. to administer the

synergistic anthelmintic compositions of Forster et al. One would have been motivated to do so since Ludwig teaches that the advantages of the bolus device include the lack of undesired chemical residues in animals used for human food production as well as the advantage that the controlled release formulation does not expose the host animal to lethal doses of the active agent (see column 2, lines 8-20).

The aforementioned references do not teach that the duration of exposure comprises at least 3 days and no more than 6 to 8 days as required by claim 29. However, Chou is directed to a slow release bolus for the controlled delivery of veterinary medicaments in ruminant animals including sheep (see abstract, in particular; see also, claim 1, line 17). Chou specifies that the boluses release a therapeutically active substance for a period of up to about 15 days in duration (see column 1, lines 58-62), including a period preferably of about 4 days (see column 3, line 15; column 6, lines 15 and line 33).

Both Forster and Chou are directed to the controlled delivery of anthelmintic active agents. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to adjust the bolus release duration as taught by Chou (i.e., by adjusting the disintegrant as taught by Chou). One would have been motivated to do so since Chou teaches that this time period for administering an extended release bolus was known to be effective to provide delivery for a case of a disease where only a relatively short period of non-immediate release into the rumen of a ruminant animal would have been desirable.

None of these references teaches the particular dosage of albendazole as in pending claims 29 and 30.

However, the IVS Annual Index teaches that 4.75 mg/kg of albendazole is an effective dosage quantity for rendering anti-parasitic effects in sheep.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the dosage quantity of albendazole as taught by the IVS Annual Index in the formulations of Forster et al. and Ludwig et al. and to optimize this value as necessary, including rounding the value of 4.75 mg/kg to 5 mg/kg/day in order to achieve the desired product strength. See MPEP 2144.05 regarding routine optimization procedures as well as Titanium Metals Corp. v. Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985). One would have been motivated to do so in order to impart the known benefits of such a dosage while expecting to minimize harmful side effects of an overdose, particularly since the artisan would have considered the IVS Annual Index a reference source for dosage details associated with known active agents such as anti-parasites, and, more specifically, albendazole.

These references do not teach the abamectin dosage as recited in claims 29 and 30.

Jeannin et al. teaches methods for removing parasites and ectoparasites from mammals (see abstract, in particular). The Jeannin reference indicates that abamectin is among equivalent preferred parasiticides (see column 3, lines 38-40) and that the effective dose administered in the method of the invention is preferably between 0.001, preferentially 0.01, and 100 mg/kg of animal weight or

0.01 to 15 mg/kg/day of endectocide (see column 3, line 65 - column 4, line 3; see also column 6, lines 20-22). It is noted that these ranges include and render obvious the data point (or range) which is "about 0.18 mg/kg/day" of abamectin as recited in claim 30. The Jeannin reference further specifies that the dosage amounts vary in order to maintain a serum level which can be adjusted to combat fleas (lower serum level) or ticks (higher serum level) for an animal of a specified mass (see column 4, lines 2-18).

Both the Forster and Jeannin references are directed to methods of reducing parasite presence. Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to optimize the quantity of abamectin to be administered to the animals per kg of body weight per day, based on the teaching of Jeannin et al., with the reasonable expectation of success. One would have been motivated to do so as it is routine inquiry in the art to minimize cost and harmful side effects while maximizing benefits. See MPEP 2144.05. One would have been motivated to utilize dosage quantities near the lower end of the dosage range specified by Jeannin et al. in order to combat fleas (parasites) by maintaining a relatively low serum level in accordance with Jeannin's teaching.

Maintained Grounds of Rejection

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude"

granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3, 15, and 16 provisionally are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 and 20 of copending Application No. 11908708. Although the conflicting claims are not identical, they are not patentably distinct from each other because all the features of instant claim 1 are included in copending application claims 1-4 which outline a composition included in the instantly claimed method, although the copending application further limits the formulation components and expands the time period of active agent release. Likewise, claims 15 and 16 of the instant invention are drawn to the same subject matter as claims 1 and 2 of the copending application, where the duration of active agent release is obvious in view of the copending application. Further, it would have been obvious to the ordinary artisan to optimize the formulation components to

achieve sufficient and desirable effects of the active/beneficial agent while minimizing negative side effects (i.e., toxicity), as instantly claimed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant's arguments presented 6/16/2011 have been fully considered but are moot in light of the new grounds of rejection set forth above. As noted above, all rejections previously presented and not re-iterated herein are withdrawn. Applicant's positions against cited references are summarized and responded to as follows.

Applicant argues that the rejection of record does not teach the newly added limitation in which the duration of exposure comprises at least 3 days and no more than 6 to 8 days. Applicant's arguments are unpersuasive in view of the above new grounds of rejection necessitated by amendment. As articulated above, the Chou reference has been applied to meet this newly added limitation. Consequently, Applicant's argument that the prior art references fail to teach or suggest all the limitations of the claims is unpersuasive.

Applicant further argues that the cited references do not indicate the instantly claimed effective daily dose in sheep. The rejection above has been clarified to address this concern more explicitly, and it is noted that the Chou reference teaches anti-parasites in sheep.

Applicant takes the position that the proposed combination would render Forster unsatisfactory for its intended purpose since Forster has been broadly stated to be useful in dogs while Ludwig teaches formulations and dosages for sheep. This position has been fully considered but is not persuasive since the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In the instant case, it is maintained that it would have been obvious to use a bolus device and method of administering anthelmintic agents to administer a combination of anthelmintic compositions because the use of bolus devices in was well known in the art (Ludwig and Chou), as was the idea of administering antihelmintics in combination (Forster). The combination of these known prior art elements would have been expected to yield predictable results because there is no reason to expect that any of the elements would have functioned differently when used in the combination. As to Applicant's subsequent argument that the daily dose of anthelmintic taught by Ludwig is inconsistent with doses of abamectin in dogs as taught by Forster, it is the Examiner's position that the combination of references together with the skill of the ordinary artisan would have allowed the ordinary artisan to select a dosage of a known anthelmintic depending on the animal to which said dosage would have been administered. Forster is relied upon for

teaching the particular anthelmintic compounds and their known applications as anti-parasites actives.

It is maintained that Lau is relied upon as an evidentiary reference and not a prior art reference, and the rejection above has been clarified to eliminate any confusing language suggesting that Lau was relied upon as prior art. The Examiner thanks Applicant for assisting in clarifying this issue.

Applicant asserts that evidence of unexpected advantages rebut any *prima facie* case of obviousness. This position has been fully considered but is not persuasive in view of the new grounds of rejection necessitated by amendment, wherein the new grounds of rejection establishes a strong case of obviousness over the claimed method. It is not apparent that the properties of the claimed invention vs. the properties of the prior art differ to such an extent that the difference really is unexpected. Moreover, Applicant has not met the burden of establishing that the differences in results relied upon are of statistical significance (see MPEP 716.02 (b)). Consequently, Applicant's arguments that secondary references (Whitehead for claim 20, IVS Annual Index for claim 12, Sanyal for claim 13, and Jeannin for claim 9) do not cure the alleged deficiency of the independent claims are unpersuasive.

Conclusion

No claims are found allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**.

See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AUDREA BUCKLEY whose telephone number is (571)270-1336. The examiner can normally be reached on Monday-Thursday 7:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fereydoun Sajjadi can be reached on (571) 272-3311. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/AJB/

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